

PATENT
5002-1074

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Manuela GUGLIELMO et al.

Conf. 8261

Application No. 10/537,296

Group 1619

Filed June 2, 2005

Examiner B. Gullledge

PREPARATION FOR TOPICAL USE WITH THE FUNCTION OF COMBATING
HAIR LOSS

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Daniela MONTANARI, one of the inventors of
the above identified application do hereby declare:

I am a Biologist, head of the Research & Development
Department of Labo Europa located in Padova, Italy. My
curriculum vitae are attached herewith.

I am familiar with the present application, and I
have reviewed the outstanding Official Action of May 26, 2009.
In doing so, I have reviewed the written description rejection
of claims 11-14 and the obviousness rejection of claims 8-14
over DESJONQUERES, HIRAMA et al., and ZAVERI et al.

I make this declaration in support of the present application and to provide evidence in rebuttal of several contentions set forth in the outstanding Official Action.

The preparation of the claims of the instant application were formulated with the precise aim of to act on the main mechanisms that cause hair loss, making precise rational choices on the basis of in-depth scientific knowledge. The claimed preparations were formulated and produced to carry out specific and particular actions, aimed at contrasting some of the mechanisms that are responsible for hair loss.

The compositions of claims 8, 11, and 14 are objectively different from many other similar hair products used to treat hair loss. The base for many hair products used to combat hair loss constitute the use of vasoactive substances, such as nicotinate. Nicotinate stimulates vasodilatation and the passage of oxygen and nourishing substances to the hair bulb.

Other substances, which are sometimes added to these hair products, include: vitamins, microelements, amino acids and sulphides, in an attempt to provide the hair with substances that are used to reconstruct the keratin fibers that the hair stem is formed of.

Other products tend to exploit the presumed action of plant extracts, which boast, without any reliable demonstration, a stimulating action for hair growth.

In the composition of the instant application, not only is the formulation original for the functional substances that are used, but there is also a theoretic rational structure that led to the choice of the functional principles of the claimed composition.

The aim of the formulation of the claimed composition is to interfere with the numerous mechanisms that cause hair loss, but without exerting any local pharmacological or systemic action, which would be the case with an anti-hormone activity.

Upon analyzing the claimed composition in the instant specification, it is shown that the two amino acids used, hydroxyproline and aspartic acid, have the task of improving the environment that houses the hair follicle: the dermal connective tissue. See, e.g., page 4, lines 20-29 and page 5, lines 33-34 of the instant application.

These two amino acids can cause an increase both in the number of fibroblast cells and in the biosynthesis of the factors produced by the dermal cells, like those that form the hair papilla. This supports the position that the specification provides full written description support for the combination of hydroxyproline and aspartic acid together,

without being complexed with silanol, in the claimed composition for topical administration to treat/delay hair loss.

The hair follicle is surrounded in its outermost part by a sheath of connective type composed of connective tissue, connected to the dermal papilla. Bundles of elastic and collagen fibres and fibroblasts responsible for the production of these proteins are present therein.

Hydroxyproline, one of the three amino acids that make up collagen (a structural protein present in the connective component of the follicle), plays an essential role in its synthesis and its stability, and gives it strength.

During collagen synthesis, after the procollagen fibrils have been formed, there is an increase in covalent crosslinking between amino acids, including hydroxyproline and aspartic acid and hexose molecules; gradual consolidation of the strength and stability of collagen thus takes place.

Aspartic acid is a highly abundant component of elastin. Elastin is a protein present in all tissues that need to be both strong and elastic in order to function, and is also present in the connective component of the follicle.

Aspartic acid is also the precursor of lysine, methionine and arginine, which are fundamental amino acids of hair biochemistry. These are the amino acids mainly represented in hair keratin.

Hydroxyproline and aspartic acid, besides being structural amino acids of the collagen and elastic fibres present in the follicle, are polar amino acids and contribute towards maintaining the hydration of proteins, and as such, also those proteins making up the follicle structure in which the hair bulb is housed, maintaining optimal trophism and structural elasticity.

The instant specification discloses that when these two ingredients, hydroxyproline and aspartic acid, are complexed with an organic by-product of silicone (silanol), it forms a substance that acts by promoting fibroblast proliferation on one side and increases the crossed links between the collagen fibers that form the dermal tissue on the other side.

Silanol, when complexed with aspartic acid and hydroxyproline, achieves complex mucopolysaccharides that are the fundamental substance in the derma.

This allows a positive interaction with the dermal tissue surrounding the hair, creating a microenvironment rich in substances that guarantee adequate support for hair growth arid, and at the same time, stimulates the dermal papillary cells that the impulse for which hair re-growth depends.

The claimed composition also includes octylbutyrate, i.e., an ester of octanol and butyric acid, and peptides that are rich in glutamine.

The addition of these two substances to the product satisfies the need to act on both the keratinisation process of the hair stem and to provide a highly energetic substratum that is useful for rapidly growing and differentiating cells, like those in the hair follicle.

In fact, octyl butyrate, stimulates the activity of the transglutaminase enzyme that is needed in the epidermis and in the hair follicle for the correct keratinisation processes. See, e.g., the discussion in the instant application at page 6, lines 15-38. Octyl butyrate also contributes towards enhancing the anchoring of the hair at its site of attachment, i.e. the hair follicle.

In the hair follicle, transglutaminases stabilize the crosslinks between the lysine and glutamine residues, for the purpose of constructing bridges between the various structural proteins. This protein/protein bonding is necessary during the skin keratinization process. In particular, octyl butyrate stimulates the synthesis of transglutaminases in the keratinocytes present in the follicle.

In particular, this enzyme is contained in the hair follicle in the internal epithelial sheath and it determines the formation of crossed links between the residual amino acids of lysine and glutamine among the structural proteins of the hair, strengthening the stem.

Thanks to the action of the transglutaminase on the glutamine, peptides rich in this amino acid have been included in the claimed formula, because glutamine is the main substratum that the enzyme works on. Furthermore, this amino acid is a fundamental energy reserve for the cellular metabolism and is used when the source of glucose has run out.

To guarantee this backup energy (that is essential for cellular growth and differentiation), another substance (which is panthenol) is added to the claimed formula. Panthenol is the essential constituent of Coenzyme A, and is a fundamental molecule for energetic metabolism in all cells of an organism, especially skin cells.

Based on the above, it is clear that the preparation of the claims of the instant application were formulated with the precise aim of to act on the main mechanisms that cause hair loss, making precise rational choices on the basis of in-depth scientific knowledge. In fact, the claimed preparations were formulated and produced to carry out specific and particular actions, aimed at contrasting some of the pathogenic mechanisms that are responsible for hair loss. Moreover, it is clear that the presence of the amino acids, hydroxyproline and asparatic acid, even without silanol, maintain the function of the connective tissue structure surrounding and supporting the hair follicle.

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I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.



Dr. Daniela MONTANARI

23.10.2009

Date